

Page 9, replace the paragraph beginning on line 25 as follows:

B2  
~~-(i) A peptide consisting of the amino acid sequence 1-93 encoded by Sequence ID No. 1 of the Sequence Table and binding calcium thereto. --.~~

Page 10, replace the paragraph beginning on line 1 as follows:

B3  
~~-(ii) A peptide consisting of the amino acid sequence 1-114 encoded by Sequence ID No. 2 of the Sequence Table and binding calcium thereto. --;~~

Page 10, replace the paragraph beginning on line 4 as follows:

B4  
~~-(iii) A peptide having an amino acid sequence in which one or more amino acids are deleted from or added to the amino acid sequence encoded by Sequence ID No. 1 or 2 of the Sequence Table, or one or more amino acids in the amino acid sequence encoded by Sequence ID No. 1 or 2 are replaced with other amino acids, binding calcium thereto, and exhibiting the activity of increasing secretion of granules of cell lines having granule secretion capability. --.~~

Page 11, replace the paragraph beginning on line 26, bridging page 12, as follows:

B5  
~~-The cells having granule secretion capability separated from blood are incubated in a RPMI 1640 medium, MEM (Minimum Essential Medium) medium, or the like which contains fetal bovine serum. Suspended cells are re-suspended in the buffer solution containing potassium chloride and sodium chloride. In the case of adhered cells, supernatant of the~~

BS  
conclude

culture liquid is discarded and cells are re-suspended in the buffer solution containing potassium chloride and sodium chloride. The suspension is incubated in the same manner as described above and processed to make the membranes permeabilized cell membranes. ]--.

Page 12, replace the paragraph beginning on line 23 as follows:

B6

--Treatment of cells using short electric pulses (an electroporation method) is another preferable method of forming permeabilized cell membranes. Specifically, an amount of  $1 \times 10^7$  cells/ml of cell line is treated with 1-10 KV (kilovolt) electric pulses at 4-40°C for 1-30 minutes. ]--.

Page 16, replace the paragraph beginning on line 5, bridging page 17, as follows:

B7

--As a method of causing calgranulin to over-expression, a method of recombining a gene encoding calgranulin in a known plasmid vector or virus vector, and introducing the recombinant into the cells can be given. The polynucleotide sequence shown as Sequence ID No. 1 or No. 2 in the sequence table, for example, can be used as a gene encoding calgranulin. The recombinant vector can be introduced into the cells by the calcium phosphate method, the DEAE dextran method, lipofectin method, electric pulse method, or the like. The above-described various methods may be preferably used for introducing a calgranulin gene in a cell line and causing the calgranulin to over-expression. The cells are converted to cells having the above-mentioned permeabilized cell membrane and a water-soluble calcium compound is preferably introduced in the cell line.

B7  
conclude

Specifically, a calgranulin gene is introduced into cells by incubating a plasmid vector or virus vector in which the calgranulin gene has been incorporated in the amount of the 1-200  $\mu\text{g}$  per  $0.5 \times 10^7$  to  $3 \times 10^7$  cells at 4-40°C for 5-120 minutes together with 1-100  $\mu\text{g}$  of calcium phosphate, 0.1-10 mg of DEAE dextran, or 1-100  $\mu\text{g}$  of lipofectin, or by treating the plasmid vector or virus vector in which the calgranulin gene has been incorporated in the amount of the 1-200  $\mu\text{g}$  per  $0.5 \times 10^7$  to  $3 \times 10^7$  cells using a short electric pulse at 4-40°C for 1-30 minutes. The above-mentioned various methods may be used for introducing the water-soluble calcium compound. --.

Page 21, replace the paragraph beginning on line 6 as follows:

B8

--The step B) for causing the sample to contact with the cell lines having granule secretion capability may be carried out before, after, or during step A) for increasing an active form of calgranulin. --;

Page 21, replace the paragraph beginning on line 14 as follows:

B9

--The same procedure as described above can be employed in the method of conducting step A) to increase active form of calgranulin of cell lines having granule secretion capability. Specifically, the following methods can be given:

a) A method of converting cell membranes of cell lines having granule secretion capability, preferably neutrophils or neutrophil-like cultured cells, into permeabilized cell membranes, and simultaneously or successively adding a calgranulin and a water-soluble calcium compound. --.

Page 22, replace the paragraph beginning on line 8 as follows:

B10  
~~—~~In the step B) of causing a sample which may contain a substance inhibiting or activating the granule secretion reaction to contact with the cell lines having granule secretion capability, and incubating the mixture, biological components, naturally occurring substances, compounds, and the like can be given as examples of the sample. This procedure of causing the sample to contact with the cell lines having granule secretion capability is carried out before, after, or during step A) of increasing an active form of calgranulin. As the cell lines having granule secretion capability, the said cell line having granule secretion capability itself, a cell line in which the calgranulin has been increased, a cell line in which the active form of calgranulin has been increased, and the like can be used. The former two cell lines increase an active form of calgranulin by the above-mentioned treatment for increasing the active form of calgranulin. ~~—~~

Page 36, replace the paragraph beginning on line 9 as follows:

B11  
~~—~~The results are shown in Table 1. The secretion inhibiting rate of samples was determined by comparison with a control which does not contain the screening sample, assuming that the secretion from the control is 100%. Compound 1 and Compound 2 decreased the activity of calgranulin A and remarkably controlled granule secretion in a system in which the amount of elastase secretion from neutrophils has been remarkably